160

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43-Y

d-Dihydro-lysergic acid diethylamide (V-A-24).

These experiments were carried out to determine if d-dihydro-lysergic acid diethylamide (V-A-24) has psychotomimetic properties, and to assess roughly its potency in this respect as compared with LSD-25. V-A-24 is known to be about one-half as potent as LSD in blocking serotonin-induced contractions of the isolated uterine muscle of the rat. No previous human trials were known.

METHODS

Subjects. All the subjects were nontolerant former morphine addicts who were serving sentences for violation of the Federal narcotic laws. All were physically healthy and none presented any of the major psychoses.

General Conditions. Subjects entered a special ward on the night before experiments were conducted. During the experimental day they could remain in their own rooms or mix with other patients in a common day room.

B-24

Drugs. d-Dihydrolysergic acid diethylamide was given in solution at 8 a.m. with the patients fasting. Preliminary experiments were conducted in which single patients received V-A-24 in doses increasing from 0.5 to 5.0 mcg/kg. The proper dose range was found to be 3.0-5.0 mcg/kg, so that all 12 patients were given these doses in a randomized balanced order. Placebos were not done. For comparison, data on 9 patients who received 1.0 and 1.5 mcg/kg of LSD-25 in another experiment are included.

Observations. Observations were made at hourly intervals once before and eight times after administration of the drug. The standard routine of the Addiction Research Center for drugs of the LSD type was used. The observations included systolic blood pressure, pupillary diameter, and threshold for the kneejerk. The change after drug was calculated by subtracting the average of the pre-drug observations from the values at each hour after drug. The areas under the time-action curve composed of these areas was calculated by the method of Winter and Flataker (1). The number of responses on the questionnaire which were not scored positively before the drug were counted. "Clinical grades" were assigned by the system of Isbell et al (2), and were based on short psychiatric examinations performed at intervals after the drug.

RESULTS

The results are tabulated in Table 1. They show that V-A-24 induces a pattern of change similar to that caused by LSD; but is, of course, less potent. From the data, it appears that V-A-24 is roughly slightly less than one-third as potent as LSD.

The mental phenomena after V-A-24 were similar to those reported after LSD and included nervousness, anxiety, a sense of strangeness, haptic sensations, visual perceptual distortion, and, in sensitive patients, visual hallucinations.

SUMMARY

1. d-Dihydro-lysergic acid diethylamide is a psychotomimetic drug. It is about one-third as potent as LSD.

B-24

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B-243

B-242

Table 1.

Comparison of the Effects of d-Dihydro-lysergic acid diethylamide and LSD-25.

MEASURE	DRUG AND DOSE (mcg/kg)				
	Placebo[1]	LSD-25[1] 1.0	LSD-25[1] 1.5	V-A-24[2] 3.0	V-A-24[2] 5.0
Pupillary Size	0.2 ± 1.4	10.2 ± 1.18	+15.0 ± 2.1	+ 8.0 ± 1.7	+12.1 ± 1.7
Blood Pressure	15.6 ± 13.5	+64.8 ± 10.9	+94.6 ± 17.5	+ 69.1 ± 24.1	85.6 ± 12.1
Patellar Reflex	+20.7 ± 11.1	-50.9 ± 31	-72.9 ± 21.7	-68.7 ± 15.4	91.1 ± 22.9
Number of Positive Responses on Questionnaire	0.1 ± 0.3	57 ± 23.2	98 ± 26.6	15.5 ± 6.4	38.7 ± 15.6
Clinical Grade	0 ± 0	2.2 ± 0.38	2.8 ± 0.17	0.83 ± 0.27	1.5 ± 0.48

1. Figures are means ± standard errors of observations on 9 subjects.
2. Figures are means ± standard errors of observations on 12 subjects.